

## **REMARKS**

### **I. STATEMENT OF SUBSTANCE OF INTERVIEW UNDER 37 CFR 1.133(B)**

Applicants' Representative thanks Examiner C. Hibbert and Primary Examiner N. Vogel for the helpful and courteous Examiner Interview held on October 14, 2009. During the Examiner Interview, Applicants' Representative presented arguments and proposed amendments to overcome the objections to the specification and claims and to overcome the rejections for indefiniteness and obviousness. The substance of the discussion is set forth in more detail below.

### **II. INFORMATION DISCLOSURE STATEMENT (IDS)**

Applicants have resubmitted the Paul et al. reference in a supplemental IDS including the missing date.

### **III. DISPOSITION OF THE CLAIMS**

Claims 1-20 were pending. Claims 1, 3, 6-7, and 9 have been amended. Claims 21-22 have been added. Claims 13-20 are withdrawn as non-elected. Upon entry of this amendment, claims 1-22 will be pending, and claims 1-12 and 21-22 will be under examination.

Applicants note that claims 11-12 should not be considered withdrawn as non-elected, because claims 11-12 are part of elected Group I. Instead, upon allowability of the elected species of claim 12, search and examination should be expanded to include claims 11-12.

No new matter has been added. As explained during the Examiner Interview of October 14, 2009, the amendment to claim 1 adding limitation "outer surface" is supported by the specification.

"While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure." M.P.E.P. 2163.I.B. In the context of support in an earlier-filed application, the Federal Circuit has stated the standard for descriptive support as follows: "[T]he test for sufficiency of support in a parent application is whether the disclosure of the application relied upon 'reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter.'" Ralston

Purina Co. v. Far-Mar-Co, Inc., 772 F.2d 1570, 1575 (Fed. Cir. 1985) (quoting In re Kaslow, 707 F.2d 1366, 1375 (Fed. Cir. 1983)).

Here, the present specification meets the standard for supporting the limitation “outer surface”. The present specification refers throughout to properties of the outer surface, including “adsorption”, surface area, and observations by microscopy. Applicants reproduce relevant passages below from publication US 2007-0048737:

[0016] The adsorption properties of calcium phosphates in relation to nucleic acids have been exploited in chromatography on HA columns to separate and purify DNA or certain RNAs. It is important to understand that given the same

[0017] It has been proved that the distribution of the charges at the surface of the solid and its hydration capacities have a great influence on the adsorption of organic molecules at its surface (Norde, W., Lyklema, J., (1991)

[0052] Type P15: spherical powder having a specific surface area of 0.62 mg<sup>2</sup>/g. They were calcined at 1180° C. and their particle size is between 80-125 μm.

[0056] Examination of the spherical powders by scanning microscopy shows that they consist of grains assembled through grain boundaries. Surface irregularities exist on some of the faces of the grains at high magnification.

The term “adsorption” relates to binding to an outer surface. This contrasts with “absorption” which relates to confining material within pores. “Adsorption, the binding of molecules or particles to a surface, must be distinguished from absorption, the filling of pores in a solid.” See <http://www.rpi.edu/dept/chem-eng/Biotech-Environ/Adsorb/adsorb.htm>. It does not appear that specific surface area includes inner surfaces such as found in pores. Finally, the specification states that features on the “faces of the grains” are identified by scanning microscopy, which could only observe inner surfaces.

Accordingly, Applicants submit that taken as a whole, the specification would convey to a skilled artisan the subject matter of “outer surface”.

#### IV. OBJECTIONS

The Office asserted that the Declaration and Application Data Sheet (ADS) are defective as referring to different filing dates. Office Action, page 4, lines 16-17.

Applicants have considered the following statement in the Declaration, page 1, referring to the international filing date followed by the US application number and PCT application number:

... the specification ...  
was filed on 12/24/2003 as United States Application Number or  
PCT International Application Number 10/540,854  
(PCT/FR2003/003897) and was amended on \_\_\_\_\_ (if applicable).

Applicants submit that the statement quoted above, while perhaps not well phrased, sufficiently identifies the referenced specification for the purposes of an inventor oath or declaration. The quoted passage identifies the specification as corresponding to US application 10/540,854 and PCT/FR2003/003897, while referencing the filing date (12/24/2003) of the PCT application.

Applicants note that the US application is the national stage of the PCT application, as identified in the ADS. The ADS also identifies 12/24/2003 as the filing date of the PCT application. Considered together, the declaration and ADS are thus fully consistent and should not be considered defective.

The Office requested a “Brief Description of the Drawings” section for Figures 1-2. Such a section has been introduced at page 9, line 9.

The claim objections have been obviated by replacing “c)” with “and c)” in claim 1, line 8, as suggested by the Office, and by replacing “to its surface” with “to an outer surface” in claim 1, line 9.

## V. INDEFINITENESS

Regarding claims 3 and 6, the indefiniteness rejection has been obviated by deleting the “preferably about 37°C” limitations. Applicants have added dependent claims reciting the deleted subject matter of temperature that is “about 37°C”.

Regarding claim 7, the indefiniteness rejection has been obviated by amendment (“~~the~~ extracellular fluids”) deleting “the”.

Regarding claim 9, the indefiniteness rejection has been obviated by amending claim 9 to recite “The method as claimed in claim 7 ~~to attach DNA~~ wherein steps b) and c) occur under physiological pH conditions ~~to calcium phosphate particles~~”.

## VI. OBVIOUSNESS

The claims stand rejected under 35 U.S.C. § 103(a) as obvious over a single reference WO 02-085330 (Troczyński).

The Office recognizes that WO 02-085330 fails to disclose (1) a 0.12 M phosphate buffer of pH 6.8 according to claim 2, (2) DNA that is plasmid, and (3) attachment of the DNA to the particle surface. Office Action, page 11, last 3 paragraphs.

Regarding item (3) relating to attachment at the particle surface, Applicants have amended claim 1 to recite “an outer surface of the particles” and thereby further distinguish WO 02-085330 as suggested in the Office Action (page 11, lines 1-3) and as discussed during the Examiner Interview of October 14, 2009.

WO 02-085330 could not render obvious the omitted feature of attachment at an outer surface, because this reference relates exclusively to encapsulating various substances, including DNA, inside a layer of calcium phosphate material.

WO 02-085330 discloses “encapsulation, and subsequent controlled release” of therapeutically active agents from “coatings and microspheres” (Abstract, lines 7-8). WO 02-085330 states (page 1, lines 4-6, and page 13, lines 13-14; emphases added):

This invention relates to novel room-temperature process for obtaining calcium phosphate, in particular hydroxyapatite,

microspheres and coatings with encapsulated drugs, proteins, genes, DNA for therapeutical use.

As a result of this protocol, a 10-1000  $\mu\text{m}$  large, nano-to-submicron porous CPC-HA microspheres matrix encapsulating the drug material is achieved.

This reference nowhere discloses attachment of a pharmaceutically active agent to an outer surface of particles. Indeed, the encapsulation disclosed in WO 02-085330 could at most be interpreted as yielding some form of attachment at an inner surface of a particle.

Applicants note the following further distinctions over WO 02-085330 to support patentability. The present invention is aimed at a process allowing the attachment of DNA molecules in plasmid form to the surface of ceramic particles. In other words, the particles according to the invention are treated by fritting at high temperature, whereas WO 02/085330 particles are obtained by precipitation.

As a result, D1 particles are formed as a network of crystals not linked by joints and thus are less dense and stable.

In addition, particles obtained by precipitation are more soluble compared to ceramic particles.

As a consequence, particles of WO 02/085330 encapsulates DNA but it is difficult to foresee what this encapsulation does to the integrity and functionality of DNA molecules.

This is not a pitfall encountered in the particles according to the present invention since DNA molecules cannot be encapsulated in ceramic. They are attached to the surface of the particles and attachment prevents degradation in cell organs having low pH as well as by nucleases of the cell cytoplasm.

Another advantage of the present invention is to allow liberation of the DNA molecules when the pH of the environment changes, which liberation is not possible in particles encapsulating the DNA like WO 02/085330 particles.

For the above reasons, Applicants submit that WO 02-085330 would not lead a skilled artisan to attach plasmid DNA to an outer surface of particles as defined in the present claims. Accordingly, Applicants request withdrawal of this ground of rejection.

**CONCLUSION**

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By 

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